Dose Escalation/Expansion Study to Investigate the Safety, Pharmacokinetics, Food Effect, and Antitumor Activity of BGB-290 in Patients with Advanced Solid Tumors

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Background

Poly (ADP-ribose) polymerase inhibitors (PARPis) represent a class of antitumor agents that exert their cytotoxic effects by inhibiting PARP activity. Some PARPis are capable of trapping PARP proteins on DNA further augmenting cell death. BGB-290 is a potent and selective PARP1/2 inhibitor with strong PARP-trapping and antitumor activity in both *in vitro* and *in vivo* preclinical tumor models harboring *BRCA* gene mutations or other homologous recombination defects.

Methods

This two-staged study (NCT02361723) consists of a Phase 1A dose-escalation/dose-finding component to establish the maximum tolerated dose (MTD) and/or recommended Phase 2 dose (RP2D) of BGB-290 in patients with solid tumors and a two-part Phase 2 component that includes expansion in targeted indications (Part A) and the effect of food on the BGB-290 pharmacokinetic (PK) profile (Part B).

Results

As of 1 May 2017, Phase 1A had completed enrollment (n=45); 3 patients remain on treatment. Objective responses were observed across the dose range (2.5–120 mg BID). Of the 23 evaluable patients with gynecological cancer, 10 (43%) achieved an objective response per RECIST 1.1 (n=3 complete; n=7 partial). More patients with germline *BRCA 1/2* mutated ovarian cancer achieved an objective response (n=7/12, 58%) than patients not carrying the mutation (n=2/8, 25%). Drug-related adverse events (AEs) reported in ≥10% of patients were nausea, fatigue, anemia, vomiting, diarrhea, anorexia and neutropenia. Anemia and neutropenia were the most common drug-related Grade 3 AEs; no Grade 4 drug-related AEs were reported. Three BGB-290-related serious AEs were reported (anemia, n=2; nausea, n=1). Four deaths were associated with an AE; however, none were considered drug-related. The BGB-290 RP2D was determined as 60 mg BID and is being evaluated in Phase 2 to determine antitumor activity and food effects. Dose escalation to determine MTD with QD dosing is ongoing.

Conclusions

BGB-290 has demonstrated a favorable safety profile and promising preliminary antitumor activity in phase 1A; phase 2 is ongoing evaluating in patients with ovarian, breast, prostate, gastric and small cell lung cancer.

Clinical trial identification

NCT02361723, January 29, 2015